# **Complete Summary**

#### **GUIDELINE TITLE**

Diagnosis and treatment of chest pain and acute coronary syndrome (ACS).

# BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of chest pain and acute coronary syndrome (ACS). Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Oct. 76 p. [121 references]

#### **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of chest pain and acute coronary syndrome (ACS). Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Oct. 78 p.

#### \*\* REGULATORY ALERT \*\*

## FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s)/intervention(s) for which important revised regulatory information has been released.

- June 15, 2005, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs): U.S. Food and Drug Administration (FDA) recommended proposed labeling for both the prescription and over the counter (OTC) NSAIDs and a medication guide for the entire class of prescription products.
- April 7, 2005, Non-steroidal anti-inflammatory drugs (NSAIDS) (prescription and OTC, including ibuprofen and naproxen): FDA asked manufacturers of prescription and non-prescription (OTC) non-steroidal anti-inflammatory drugs (NSAIDs) to revise their labeling to include more specific information about potential gastrointestinal (GI) and cardiovascular (CV) risks.

#### **Additional Notices**

- August 16, 2007, Coumadin (Warfarin): Updates to the labeling for Coumadin to include pharmacogenomics information to explain that people's genetic makeup may influence how they respond to the drug.
- June 8, 2007, Troponin-I Immunoassay: Class I Recall of all lots of the Architect Stat Troponin-I Immunoassay. The assay may report falsely

- elevated or falsely decreased results at and near a low level, which may impact patient treatment.
- <u>December 8, 2006, Heparin Sodium Injection</u>: Revisions to the WARNINGS section of the prescribing information for Heparin to inform clinicians of the possibility of delayed onset of heparin-induced thrombocytopenia (HIT), a serious antibody-mediated reaction resulting from irreversible aggregation of platelets.
- October 6, 2006, Coumadin (warfarin sodium): Revisions to the labeling for Coumadin to include a new patient Medication Guide as well as a reorganization and highlighting of the current safety information to better inform providers and patients.

## **COMPLETE SUMMARY CONTENT**

\*\* REGULATORY ALERT \*\*

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

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IDENTIFYING INFORMATION AND AVAILABILITY

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#### **SCOPE**

## DISEASE/CONDITION(S)

- Chest pain/discomfort, including coronary artery disease (CAD) and noncardiac causes
- Acute myocardial infarction
- ST-elevation myocardial infarction

#### **GUIDELINE CATEGORY**

Diagnosis

Evaluation

Management

Rehabilitation

Risk Assessment

Screening

Treatment

# CLINICAL SPECIALTY

Cardiology Emergency Medicine Family Practice Internal Medicine Surgery

#### INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Nurses
Physician Assistants
Physicians

## GUIDELINE OBJECTIVE(S)

- To increase the success of emergency intervention for patients with high-risk chest pain
- To minimize the delay in administering thrombolytics or angioplasty to patients with acute myocardial infarction (AMI)
- To increase the timely initiation of treatment to reduce postinfarction mortality in patients with AMI
- To increase the percentage of patients with AMI, who have used tobacco products within the past year, who receive tobacco use assessment and cessation counseling and treatment within 24 hours of admission
- To improve the diagnostic value of stress tests through their appropriate use in patients with chest pain symptoms
- To increase the percentage of patients with AMI using appropriate cardiac rehabilitation post-discharge
- To increase the percentage of patients with AMI whose course of treatment has followed the recommended critical pathway
- To increase the use of risk stratifying procedures in patients with AMI

## TARGET POPULATION

Adults greater than age 18 years presenting with past or present symptoms of chest pain, discomfort, and/or indications of acute coronary syndrome (ACS)

# INTERVENTIONS AND PRACTICES CONSIDERED

## Screening/Evaluation/Diagnosis/Risk Assessment

- 1. Initial evaluation by triage
- 2. Medical history, physical examination, and risk assessment
- 3. Clinic evaluation depending on symptoms and risk factors
- 4. Vital signs assessment
- 5. Electrocardiogram (ECG)
- 6. Cardiac markers (troponin T or I, creatine kinase MB)
- 7. Diagnostic coronary angiography

- 8. Treadmill stress test
- 9. Computed tomography (CT) angiogram, echocardiogram/transesophageal echocardiography (Echo/TEE), magnetic resonance imaging (MRI), arterial blood gases, chest x-ray if indicated

# Management/Treatment/Rehabilitation

- 1. Emergency interventions including ambulance transport to Emergency Department, immediate assessment with cardiac monitoring, initial management according to the American Heart Association Advanced Cardiac Support guideline
- 2. Early therapy including an intravenous line, oxygen, aspirin (ASA), heparin/low-molecular weight heparin (LMWH), beta-blockers (esmolol) in eligible patients, clopidogrel, nitroglycerin, morphine, glycoprotein IIb-IIIa inhibitors (Tirofiban HCL, abciximab, Eptifibatide)
- 3. Percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) if indicated
- 4. Thrombolytics including tissue plasminogen activator (tPA) TNK, rPA
- 5. Treatment of acute myocardial infarction (AMI) complications
- 6. Phase 1 cardiac rehabilitation including ASA, clopidogrel, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors (angiotensin receptor blockers [ARBs] if ACE inhibitors not tolerated), calcium channel blockers, oral nitrates, LMWH, warfarin, antiarrhythmic agents, statins, tobacco cessation, glycemic control, healthy diet, and manageable exercises
- 7. Phase 2 cardiac rehabilitation (outpatient management) including medically supervised exercise with ECG monitoring, health education, risk factor modifications, and exercise prescription
- 8. Phase 3 and 4 cardiac rehabilitation (maintenance)
- 9. Follow-up

#### MAJOR OUTCOMES CONSIDERED

- Diagnostic value of tests
- Prognostic value of risk assessment interventions
- Effectiveness of secondary prevention, treatment, and rehabilitation interventions on reducing mortality and morbidity rates
- Positive predictive value of new ST elevation

#### METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

# METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

**COST ANALYSIS** 

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Clinical Validation-Pilot Testing Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Institute Partners: System-Wide Review

The guideline draft, discussion, and measurement specification documents undergo thorough review. Written comments are solicited from clinical, measurement, and management experts from within the member medical groups during an eight-week period of review period.

Each of the Institute's participating medical groups determines its own process for distributing the guideline and obtaining feedback. Clinicians are asked to suggest modifications based on their understanding of the clinical literature coupled with their clinical expertise. Representatives from all departments involved in implementation and measurement review the guideline to determine its operational impact. Measurement specifications for selected measures are

developed by the Institute for Clinical Systems Improvement (ICSI) in collaboration with participating medical groups following general implementation of the guideline. The specifications suggest approaches to operationalizing the measure.

## Guideline Work Group

Following the completion of the review period, the guideline work group meets 1 to 2 times to review the input received. The original guideline is revised as necessary and a written response is prepared to address each of the responses received from member groups. Two members of the Cardiovascular Steering Committee carefully review the input, the work group responses, and the revised draft of the guideline. They report to the entire committee their assessment of four questions: (1) Is there consensus among all ICSI member groups and hospitals on the content of the guideline document? (2) Has the drafting work group answered all criticisms reasonably from the member groups? (3) Within the knowledge of the appointed reviewer, is the evidence cited in the document current and not out-of-date? (4) Is the document sufficiently similar to the prior edition that a more thorough review (critical review) is not needed by the member group? The committee then either approves the guideline for release as submitted or negotiates changes with the work group representative present at the meeting.

#### Pilot Test

Member groups may introduce the guideline at pilot sites, providing training to the clinical staff and incorporating it into the organization's scheduling, computer, and other practice systems. Evaluation and assessment occur throughout the pilot test phase, which usually lasts for three-six months. At the end of the pilot test phase, ICSI staff and the leader of the work group conduct an interview with the member groups participating in the pilot test phase to review their experience and gather comments, suggestions, and implementation tools.

The guideline work group meets to review the pilot sites' experiences and makes the necessary revisions to the guideline, and the Cardiovascular Steering Committee reviews the revised guideline and approves it for release.

### RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the Institute for Clinical Systems Improvement (ICSI): For a description of what has changed since the previous version of this guidance, refer to "Summary of Changes -- October 2006."

The recommendations for diagnosis and treatment of chest pain and acute coronary syndrome (ACS) are presented in the form of 7 algorithms with 127 components, accompanied by detailed annotations. Algorithms are provided for: <a href="Chest Pain Screening">Chest Pain Screening</a>; <a href="Emergency Intervention">Emergency Intervention</a>; <a href="ST-Segment Elevation Myocardial Infarction">ST-Segment Elevation Myocardial Infarction</a> (STEMI); <a href="Acute Myocardial Infarction">Acute Myocardial Infarction</a> (AMI) <a href="Complications">Complications</a>; <a href="Special">Special</a>

Work-Up; Non-Cardiac Causes; and Clinic Evaluation. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.

Class of evidence (A-D, M, R, X) definitions are provided at the end of the "Major Recommendations" field.

## Clinical Highlights

- On initial contact with the health care system, high-risk patients need to be identified quickly and referred to an emergency room (ER) via the 9-1-1 system. (Annotations #1-7).
- Patients whose chest pain symptoms are suggestive of serious illness need immediate assessment in a monitored area of the emergency department (ED) and early therapy to include an intravenous (IV) line, oxygen, aspirin, nitroglycerin, and morphine. (Annotations #20 and 25)
- Triage and management of patients with chest pain and unstable angina must be based on a validated risk assessment system (i.e., American College of Cardiology/American Heart Association [ACC/AHA] criteria). (Annotation #27)
- Patients with high-risk features need to be identified quickly and treatment instituted in a timely fashion (Annotations #27-31)
- Patients with low-risk symptoms should be evaluated as outpatients in a timely fashion. (Annotations #27, 36, 37)
- Treadmill test results should be reported using the Duke treadmill score, based on the Bruce protocol (Annotations #97-103, 107, 111, 115).
- Thrombolysis should be instituted within 30 to 60 minutes of arrival, or angiogram/primary percutaneous coronary intervention (PCI) should be performed within 90 minutes of arrival with a target of less than 60 minutes. (Annotations #43, 45)
- Use of medication: aspirin and clopidogrel (Plavix®) (or clopidogrel alone if aspirin allergic) at admission. (Avoid clopidogrel if cardiac surgery is anticipated.) Beta-blockers whenever possible and/or angiotensin-converting enzyme (ACE) inhibitors at 24 hours if stable, nitrates (when indicated), and statins whenever possible. Once the issue of surgery is clarified, consider the early use of clopidogrel for those in whom PCI is planned (Annotations #25, 48, and 65)
- Recommend appropriate use of cardiac rehabilitation post-discharge. (Annotations #63 and 64)

## Chest Pain Screening Algorithm Annotations

 Initial Contact with Complaint of "Chest Pain/Discomfort" in Person or Via Telephone

Initial presentation may be in person or on the phone, etc.

#### Definitions:

Chest: Upper abdomen, chest, upper back, throat, jaw, shoulders, upper arms.

Pain: "Discomfort" or other abnormal sensation such as "gas," "indigestion," "fullness," "pressure," "tightness," or "heaviness."

Evidence supporting this recommendation is of class: R

2. Initial Evaluation by Triage Indicates Elevated Risk?

# Key Points:

• The purpose of triage is to avoid delay in the identification of acute coronary syndromes, not to diagnose common, non-emergent causes of chest pain.

Triage should move patients with suspicious symptoms forward (especially diabetic and middle-aged or older) to immediate electrocardiogram (ECG) and prompt clinician assessment (with expedited cardiac enzymes if appropriate). Triage staff should be systematically trained to recognize chest pain and cardiovascular risk indicators. Reception and other staff should bring all complaints of chest pain and breathlessness to medical personnel for further evaluation, especially when:

- The patient is currently having symptoms.
- The interviewer senses distress.
- Symptoms have been present for less than 8 weeks (or are getting worse).
- The patient feels the pain was at least moderate.
- There are other symptoms of ill health (e.g., shortness of breath, weakness, sweating, nausea).
- The patient requests an immediate opportunity to discuss the symptoms with medical personnel.

Evidence supporting this recommendation is of class: D

4. Brief Screening History by Medical Personnel

#### Key Points:

 Teach medical triage personnel to appropriately conduct the brief screening history, paying particular attention to presence of high-risk symptoms.

Angina, typical angina, atypical angina, atypical chest pain, and non-cardiac chest pain are not consistently defined and used in medical practice. Sometimes they are used to describe a symptom complex; at other times they are used to describe an etiology. For the purposes of this guideline, the following definitions will be used to categorize the patient's chest pain or discomfort as a symptom complex and not an etiology:

Typical angina - pain or discomfort that is 1) substernal, 2) provoked by exercise and/or emotion, and 3) relieved by rest and/or nitroglycerine.

Atypical angina - pain or discomfort that has two of the three features listed for typical angina.

Nonanginal chest pain - pain or discomfort that has one or none of the three features listed for typical angina.

It should be emphasized that patients with non-anginal chest pain may still be at risk for AMI or acute coronary syndrome. Several serious illnesses are included in the differential diagnosis of chest pain. Assessment of these illnesses requires office or ED evaluation. The initial phone interview is limited to determining the timing and location of the initial office or ED evaluation.

The risk of immediate adverse outcome is a function of the time course of the chest pain. If the symptoms have been stable for more than 2 weeks, the risk of an immediate adverse outcome is low. The phone history should stress symptoms suggestive of life-threatening illnesses and the time course of the symptoms.

High-Risk Symptoms

Symptoms suggestive of a high risk of immediate adverse outcome include, but are not limited to:

- Severe or ongoing pain
- Pain lasting 20 minutes or more
- New pain at rest or with minimal activity
- Severe dyspnea
- Loss of consciousness

The interviewer may use his/her discretion with respect to the need to obtain further history for such symptoms or refer to a physician.

All patients with high-risk chest pain symptoms should be instructed on the proper use of 911.

The interviewer must use his or her judgment. This guideline focuses on serious complaints that the interviewer feels may signify a serious illness. Chest pain that is not high risk in the judgment of the interviewer (e.g., a young person with chest wall pain) may be evaluated in the office.

A suggested shingle outlining the necessary documentation for this encounter is available from Institute for Clinical Systems Improvement (ICSI). See the Support for Implementation section in the original guideline document.

Teach medical triage personnel to appropriately conduct the brief screening history.

Evidence supporting this recommendation is of class: R

5. High-Risk Symptom(s) Present at Time of Call

## 6. High-Risk Symptom(s) Present Within Last 2 Days

Patients who have had high-risk symptom(s) within the previous two days are at the highest risk and should enter the 911 system. The interviewer may judge the need for ambulance transport and office or ED evaluation for patients who call hours or days after transient symptoms resolve.

# 8. High-Risk Symptom(s) Present Between 3 Days and Last 2 Weeks

Patients who have had high-risk symptom(s) within the previous two weeks but not the previous two days may be safely evaluated in either a properly equipped office or the ED.

## 10. High-Risk Symptom(s) Present Between 2 Weeks and 2 Months

High-risk symptom(s) within two months of the initial evaluation but not within two weeks identify a group of patients at lower risk for immediate adverse outcome. These patients can be evaluated in the office within three days.

#### 11. Clinic Evaluation Within 72 Hours

Patient education directed toward use of 911 and recognition of signs and symptoms of an advancing coronary event should occur at this point.

# 12. High-Risk Symptom(s) Present More than Two Months Ago

Patients who have been stable without high-risk symptoms for the previous two months can be seen as a routine appointment.

## 13. Elective Clinic Evaluation (Within 2 Weeks)

Patient education directed toward use of 911 and recognition of signs and symptoms of an advancing coronary event should occur at this point.

## 14. Urgency Uncertain

If the severity and/or duration of the chest pain symptoms cannot be determined in the phone interview, the patient should be seen on the same day in the office or the ED.

# **Emergency Intervention Algorithm Annotations**

# 19. Ambulance Transport to Emergency Department

A patient complaining of chest pain suggestive of serious etiology should be transported via ambulance with advanced cardiac life support (ACLS)

capabilities whether he/she is being transported from home or outpatient clinic to the FD.

Patients who are critically ill or unstable should be taken to a hospital capable of performing cardiac catheterization and cardiac surgery unless this would lead to excessive transport time. Plans for triage of a critically ill patient to a tertiary care institution should be part of every community hospital plan.

If a patient is seen in a clinic or physician's office complaining of chest pain suggesting a serious condition, the patient must be transported to the ED as soon as possible. Attempts should be made to stabilize the patient as well as possible prior to transport. The referring physician must call the receiving physician and send copies of all medical records pertaining to the current illness.

Evidence supporting this recommendation is of classes: B, R

## 20. Immediate Assessment with Cardiac Monitoring

On arrival in the ED, a patient complaining of chest pain should immediately receive oxygen via nasal cannula, and a 324 mg loading dose of aspirin, preferably chewed (for patient palatability, use four 81 mg baby aspiring tablets). An immediate electrocardiogram (ECG) should be done and the physician called for as the patient is placed on a cardiac monitor. An IV should be started as soon as possible and cardiac markers drawn. Troponin I or T has been proven to be very sensitive and specific for myocardial injury as well as predictive of short-term risk for myocardial infarction or death. Creatine kinase MB band (CKMB) should no longer be used as the primary marker for myocardial infarction, but can be useful in assessing the timing of the event. It may also be useful in patients with renal failure who also have an elevated troponin. Interpretation of an abnormal serum troponin (or CKMB) is dependent upon the clinical setting in which the myocardial injury occurred. Initial brain natriuretic peptide (BNP) may be of value in assessing cardiac function. A portable chest x-ray may be performed if indicated. The ED physician should also be called to the patient's bedside immediately.

On arrival, the physician should perform a brief initial assessment based on vitals, brief historical information, and physical examination. Institution of stabilizing therapy (including chewable aspirin, nitroglycerin, and morphine for suspect anginal pain) prior to completing history or physical is appropriate and often necessary at this level.

Evidence supporting this recommendation is of classes: B, R

#### 21. Vital Signs Compromised?

In the critically ill patient whose vitals are compromised (i.e., cardiac arrest, tachyarrhythmias, severe bradycardia, shock, or hypotension); the Advanced Cardiac Life Support guideline developed by the American Heart Association should be followed.

# 22. Initiate Advanced Cardiac Life Support (ACLS) Protocols

The Consolidated Omnibus Budget Reconciliation Act (COBRA) of 1987, 1989, and 1990 places strict requirements and restrictions on initial assessment and transfer of patients with emergency medical conditions and women in labor.

The American Heart Association Advanced Cardiac Life Support guideline provides the most recent protocols for initial management of patients whose vital signs are compromised.

# 23. Symptoms Suggest Possibility of an Acute Coronary Syndrome Disease (ACS)?

The symptoms that suggest ACS are, in order of importance:

- 1. Chest pain description (See Annotation #4 above, "Brief Screening History by Medical Personnel")
- 2. History or evidence of ischemic heart disease
- 3. Age, gender, comorbidities (atypical presentation in female, elderly, and diabetic)
- 4. Presence of cardiac risk factors

The description of the patient's chest pain or discomfort is the most critical part of the history. Although multiple other features of the chest pain may be incorporated into an experienced clinician's judgment, the clinician should ultimately attempt to classify the patient as having typical angina, atypical angina, or nonanginal chest pain as described in Annotation #4, "Brief Screening History by Medical Personnel" of the Chest Pain Screening algorithm.

Evidence supporting this recommendation is of classes: C, M

#### 24. ECG Positive for ST-Segment Elevation?

### **Key Points:**

• An ECG should be obtained immediately upon arrival in the ED.

The recognition of coronary artery disease and evaluation of its severity cannot be adequately carried out without an ECG. The early performance of an ECG following arrival at the emergency department is therefore critical. When patients have new or presumably new ST elevation of greater than 1 mm in two contiguous limb leads, or equal to two mm or more in precordial leads, they should be considered to have acute myocardial infarction. Patients with new or presumably new left bundle branch block (LBBB) should be treated similarly to those with ST segment elevation. Although some patients with LBBB will prove not to have acute myocardial infarction, thrombolytic therapy of patients with LBBB is nevertheless associated with a reduction in patient mortality.

Regardless of ST elevation, consider cardiology consultation early.

Evidence supporting this recommendation is of classes: A, C, R

# 25. Early Therapy

# Key Points:

- Patients whose chest pain symptoms are suggestive of serious illness need immediate assessment in a monitored area of the ER and early therapy to include an IV, oxygen, aspirin, nitroglycerin, and morphine.
- Early therapy may consist of: aspirin, heparin or low molecular weight heparin, nitrates, beta blockers, and clopidogrel.

Aspirin (ASA) reduces mortality, reinfarction, and stroke. Although the incremental value of heparin/low-molecular weight heparin (LMWH) in conjunction with aspirin and reperfusion therapy is controversial, it does appear to enhance patency, and was included in the GUSTO protocol. In eligible patients, beta-blockers reduce mortality, reinfarction, and stroke. Although long-acting nitrates (oral and intravenous) appeared to reduce mortality in trials that did not include thrombolysis, more recent studies that did include thrombolysis found no incremental benefit from nitrate therapy. Nitrate therapy is still appropriate for ischemic pain relief.

All patients should receive aspirin (chewable) as soon as possible and continued indefinitely. In those patients who are unable to take aspirin, clopidogrel should be considered in hospitalized patients. If the probability of urgent coronary artery bypass graft (CABG) is low, consider early use of clopidogrel. The benefits of beta-blockers, nitroglycerin, and heparin are well established. There is data to support the use of LMWH as an alternative to intravenous heparin.

In high-risk patients, early administration of subcutaneous LMWH (enoxaparin 1mg/kg subcutaneous every 12 hours) or IV unfractionated heparin (UFH) (70 units/kg load then 12 to 15 units/kg/hr to achieve activated partial thromboplastin time [aPTT] levels of 1.5 to 2.5 times the control), with aspirin and/or clopidogrel is associated with a decrease in the incidence of AMI and ischemia.

LMWH, specifically enoxaparin, has been shown to have a moderate benefit over IV heparin in decreasing the rate of death, myocardial infarction (MI), and recurrent ischemia. A meta-analysis of the 2 trials showed a statistically significant reduction by 20% in the rate of death and MI.

LMWH should be used with caution in patients with renal insufficiency.

The recently completed SYNERGY study found increased adverse events in patients that were switched from unfractionated heparin to low-molecular weight heparin or vice-versa at the time of referral to tertiary care institutions. Therefore, the suggestion is that the patient be started and maintained on one drug or the other during transfer and treatment at referring and referral institutions.

Beta-blockers should be initiated early in the absence of any contraindications. In high-risk patients, they should be given initially IV, then followed by the oral route with a goal target resting heart rate of 50 to 60 beats per minute (bpm). Patients with low to intermediate risk may start out with oral therapy. The duration of benefit is uncertain. A meta-analysis of double blinded randomized trials in patients with evolving MI showed a 13% reduction in risk progression to AMI. Other multiple randomized trails in coronary artery disease (CAD) patients have shown a decrease in mortality and/or morbidity rates.

Beta-blockers should be used in most patients with STEMI. They remain underutilized in patients with chronic obstructive pulmonary disease (COPD) and diabetes mellitus where definite benefit has been demonstrated. Beta-blockers are relatively contraindicated in patients with asthma and hypotension, less so with first degree atrioventricular (AV) block, heart rate less than 60/min, or decompensated congestive heart failure (CHF). They should be used cautiously, if at all in these conditions. They should be completely avoided in STEMI due to cocaine use because of the risk of exacerbating coronary spasm, and in patients with cardiogenic shock.

Nitroglycerin should be given sublingually (0.4 mg every five minutes) to relieve ischemic symptoms. If symptoms are ongoing or recurrent despite the administration of IV beta-blockers, IV nitroglycerin can be initiated at 10 mcg/min and titrated every 3 to 5 minutes by 10 mcg/min until symptom response is noted or blood pressure decreases to less than 110 mmHg in patients previously normotensive or by 25% in patients who were hypertensive on presentation, or to a maximum dose of 200 mcg/min. Patients can be converted to topical or oral nitrates once stabilized (no manifestations of ischemia and pain free for 12 to 24 hours).

ISIS-4 and GISSI-3 failed to show a benefit of nitroglycerin on reduction of mortality in AMI.

Nitroglycerin is contraindicated in patients who are hypotensive, have documented severe aortic stenosis, have hypertrophic cardiomyopathy, or who have received sildenafil, vardenafil, or ordenafil within the previous 24 hours or tadalafil in the previous 48 hours.

## GPIIb/IIIa Inhibitors

Patients with high risk or patients with intermediate risks and diabetes as defined in Annotation #27 "Risk Assessment (ACC/AHA Criteria)," benefit from receiving GP IIb-IIIa inhibitor (Tirofiban HCI, abciximab, or Eptifibatide) as part of initial treatment.

Early invasive strategy involves diagnostic catheterization within 24 to 48 hours, followed by PCI or CABG if warranted.

Contraindications to IIb-IIIa inhibitors include bleeding less than six weeks, intracranial hemorrhage (ever), recent stroke less than 2 years, uncontrolled hypertension greater than 200/100 mm Hg, surgery less than six weeks, aortic dissection, acute pericarditis, and platelets less than 100,000 mm<sup>3</sup>.

Evidence supporting this recommendation is of classes: A, C, M, R

## 27. Risk Assessment (ACC/AHA Criteria)

# Key Points:

 Medical groups and hospitals should implement a validated risk assessment criteria set systemwide.

Low-risk patients may be safely evaluated as outpatients. These will include some patients with slight progression of their symptoms, which may reflect non-compliance with medications, increasing activity, emotional stress, or other exacerbating factors. Patients with a low likelihood of CAD on the basis of chest pain description, age, gender, and risk factor assessment, and patients at intermediate likelihood who have not had at-rest symptoms that are prolonged or accompanied by shortness of breath or other worrisome features, should also be considered stable.

For patients whose angina does not seem stable, it is important to use objective risk assessment criteria for purposes of triage (Critical Care Unit [CCU]), monitored bed, or dismissal with follow-up). This guideline endorses the criteria published by the ACC/AHA in 2002 "ACC/AHA 2002 Guideline Update for the Management of Patients with Unstable Angina and Non-ST-segment Elevation Myocardial Infarction." These consist of a simple set of clinical variables to classify patients as high-, intermediate-, or low-risk of death of MI. The work group acknowledges that many other risk assessment criteria sets exist (e.g., TIMI), and recommends that medical groups and hospitals choose one that is validated and implement its use systemwide.

Complete certainty of the etiology of a patient's chest pain can commonly not be attained in the ED. It is therefore vitally important to assess risk in order to safely and yet cost-effectively triage chest pain patients. Further, it is important to recognize the difference between risk assessment and likelihood assessment in that likelihood assessment merely serves to communicate just that, while risk assessments may be used as a tool for clinical management.

Evidence supporting this recommendation is of classes: B, C, R

# 28. High Risk

High-risk unstable angina patients require a high level of care with close monitoring and IV therapy, including heparin, beta-blockade, and nitroglycerin. This needs to be started in the ED setting. Hospitalization usually requires an intensive care unit (ICU) setting or competent nursing in a monitored bed setting.

#### 29. Early Therapy

See Annotation #25, "Early Therapy", above.

## 31. Perform Catheterization Within 24 to 48 Hours

An early invasive strategy is beneficial in many patients with non-STEMI and ACS, especially when coupled with aggressive adjunctive therapy such as unfractionated heparin with a glycoprotein IIb/IIIa antagonist or use of a low molecular weight heparin. Certainly the aggressive anticoagulation and antiplatelet agents should be utilized when there are recurrent symptoms and no ability to proceed to early angiography, such as a weather-related delay or the catheterization lab is not available. However, in patients who become unstable or have recurrent symptoms, one should minimize the delay for angiography and percutaneous coronary revascularization.

Contraindications to IIb-IIIa inhibitors include bleeding less than six weeks, intracranial hemorrhage (ever), stroke less than two years, uncontrolled hypertension greater than 200/100 mm Hg, surgery less than six weeks, aortic dissection, acute pericarditis, platelets less than 100,000 mm<sup>3</sup> and dialysis dependent renal failure.

Evidence supporting this recommendation is of classes: A, C, M, R

#### 32. Intermediate Risk

A patient of intermediate risk unstable angina (as defined by the ACC/AHA Guideline) is by far the most common presentation to the emergency department. Approximately 50% of these patients will turn out to have an end point diagnosis other than ACS. It is, however, impossible to predict which patients truly have an ACS after the initial evaluation in the emergency department. As the short-term risk of a significant cardiac event is between 5 and 20%, it is imperative to treat each patient according to protocol during the evaluation process. These patients should be considered as primary candidates for evaluation in a cardiac observation unit if available, or a critical pathway in a monitored bed setting.

## 33. Early Therapy

See Annotation #25, "Early Therapy" above.

## 34. Admit to Chest Pain Unit (CPU) or Monitored Bed

If the patient's risk assessment is not clearly in a high- or low-risk category, and the institution has an ED-based chest pain observation unit, admission to this unit would be appropriate. Otherwise, management using a critical pathway for unstable angina with a similar protocol on a monitored bed unit is recommended.

A CPU/critical pathway provides monitoring capabilities, a dedicated nurse, serial cardiac markers (markers should be negative for at least six hours from the onset of symptoms), and a post-observation stress test prior to final triage decision. Generally, after successful completion of the evaluation, patients can be classified as low-risk and safely followed up as outpatients in the next 1 to 3 days. In the case of a positive or indeterminate lab test, ECG or stress/imaging test, or if there is recurrent chest pain during the

observation period, a patient should be considered high risk and managed accordingly.

It should be emphasized that a patient who requires repeated doses of nitroglycerin and/or IV nitroglycerin or paste, or requires beta-blockade for pain control should be considered high risk.

Refer to Annotation #27, "Risk Assessment (ACC/AHA Criteria)" above for more information on risk stratification.

Evidence supporting this recommendation is of class: R

# 35. Patient Has Positive: Markers? ECG Changes? Treadmill Stress Test? Unstable Dysrhythmias?

If a patient develops recurrent chest discomfort during the observation period, the patient should be considered having failed the observation unit intervention and should be considered high risk and admitted to a monitored bed or an ICU setting. If the cardiac markers, troponin T or I, and CKMB on the second blood draw are positive, or the patient develops new or dynamic ST-T wave changes, the patient should also be considered high risk. If a patient develops an unstable dysrhythmia (i.e., ventricular tachycardia [VT] or multifocal premature ventricular contractions [PVCs], etc.), he/she should also be considered high risk and admitted.

Most patients in this category will have an uneventful observation period and should undergo an endpoint stress test. The choice of a treadmill exercise test utilizing the Bruce treadmill score should be preferred in all patients who can walk and have an interpretable ECG. In some instances additional imaging may be beneficial. Refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) guideline Cardiac Stress Test Supplement. If the patient is unable to walk, a pharmacologic stress test should be considered. Patients needing continued beta-blockade may be candidates for nuclear imaging instead of standard treadmill stress testing.

Evidence supporting this recommendation is of classes: A, C

## 36. Low Risk

Patients with a history of brief episodes of chest pain (less than 20 minutes) but suggestive of accelerating and/or class 3 or 4 angina should be considered low risk if indeed ECG can be obtained during the chest pain episodes. If, however, an ECG cannot be obtained during a chest pain episode or other atypical features are present, the patient may be managed as intermediate risk and be evaluated in a cardiac observation unit.

#### 37. Discharge to Outpatient Management

If the diagnosis is low-risk unstable angina, a follow-up appointment, preferably with a cardiologist, should be done. Otherwise, a follow-up with a

primary care physician may also be appropriate. These appointments should occur within one to three days. If the chest pain is considered stable angina and non-anginal chest pain, an arrangement for follow-up with a primary care physician should be arranged in the near future. The primary care physician may want to follow the clinical evaluation algorithm provided within the original guideline document.

#### 38. Non-Cardiovascular Chest Pain

In elevating a patient with chest pain it is important to keep in mind the entire differential diagnosis, including non-cardiac causes. Missed or misdiagnosis may have serious implications, both in regards to medico-legal issues and resource utilization.

# 39. Chest Pain Not Related to CAD, but Indicative of Other Serious Diagnosis?

Aortic dissection, pulmonary embolus, expanding pneumothorax, pericarditis with impending tamponade, or serious gastrointestinal pathology are all potentially life threatening and may closely mimic presentations of an acute coronary syndrome. Further, the presence or absence of reproducible chest wall pain does not preclude the possibility of a more serious underlying cause.

## STEMI Algorithm Annotations

## 42. ST-Segment Elevation on ECG

About 40% of patients with AMI present with ST-segment elevation. They can be treated with thrombolytics or with emergency coronary angiography and percutaneous coronary intervention. Patients presenting with chest pain but no ST-segment elevation may be triaged to the telemetry unit if they are hemodynamically stable and pain-free.

Facilities without PCI capabilities should consider establishing processes and criteria for transfer for immediate PCI.

#### 43. Thrombolytics or PCI for Initial Therapy

Indications for Thrombolytics

- ST segment elevation of 1 mm or more in two or more contiguous limb leads or
  - ST segment elevation of 2 mm or more in precordial leads or
  - New or presumably new LBBB; ST segment depression of 2 mm or more in  $V_1V_2$  (true posterior infarction), and
- Anginal chest pain between 30 minutes and 12 hours in duration that is unrelieved with nitroglycerin

When immediately available, percutaneous transluminal coronary angioplasty (PTCA) is equal to and may be superior to thrombolysis.

# Administration of Thrombolytics

Options include full dose lytic of choice (tissue plasminogen activator [tPA], TNK, rPA), half-dose lytic (transfer arrangements with the receiving institution should be worked out in advance; this is a IIb indication per the 2004 ACC/AHA guidelines), or transfer for primary PCI.

Low patient weight has been identified as an ongoing risk factor for significant intracranial hemorrhage (ICH) when thrombolytics are administered. It is imperative to accurately estimate the weight of patients with acute myocardial infarction to determine the proper dose of thrombolytic to minimize the risk of ICH.

Single-bolus agents, such as tenecteplase (TNKase®) simplify administration; however patient weight remains important in calculating dose.

Refer to the original guideline document for additional information on lytic administration.

Contraindications to Thrombolytics

Refer to the "Contraindications" field for more information.

Refer to the original guideline document for common causes of delay in initiation of thrombolytics.

### 45. Emergency Coronary Angiography and Primary PCI

## Key Points:

 Primary PCI has been demonstrated to be more effective than thrombolysis in opening acutely occluded arteries in settings where it can be rapidly employed by experienced interventional cardiologists.

Time to open artery is critical to effective primary PCI. Current ACC/AHA guidelines suggest that institutions wishing to apply primary PCI for STEMI should achieve a median door-to-balloon time of 90 minutes or less. The ACC/AHA Consensus Panels have set a 60-minute median door-to-balloon time as the benchmark for top performing institutions.

Institutions that cannot meet the recommended treatment times should consider preferential use of intravenous thrombolytic therapy. These institutions should have a predetermined plan for treating patients who present with contraindication to thrombolytics.

Aspirin, heparin, nitrates, and beta-blockers should be administered early to these patients, unless contraindicated.

Primary PCI may also play a role in the treatment of non-STEMI/refractory angina pectoris if angina symptoms fail to resolve within an hour of instituting aggressive anti-anginal therapy with aspirin, heparin, beta-blockers, and GP

IIb-IIIa inhibitors; or serial ECG or echocardiogram suggest a large amount of myocardium at risk.

For centers that have demonstrated high success rates and low complications rates, this strategy is at least equal in efficacy to that of initial thrombolytic therapy, especially for those patients at high risk of mortality, and may be considered in thrombolytic candidates, as well as in patients with thrombolytic contraindications. It is the preferred therapy for cardiogenic shock. Immediate transfer of salvageable patients to an institution capable of treating this condition is indicated for the presentation or development of cardiogenic shock.

Rescue angioplasty involves the use of PCI to restore coronary flow after thrombolysis has failed. Guidelines for time from arrival to balloon inflation are not established for this complex subset of patients, but rescue PCI should be accomplished within 90 to 120 minutes of thrombolytic failure if possible. Thrombolytic failure may be evident by failure of ST-elevation to resolve within 30 to 60 minutes of thrombolytic therapy and usually includes persistent symptoms.

Facilitated PCI is the use of additional agents to pretreat the patient awaiting primary PCI. No strategy employing full- or reduced-dose thrombolytic (with or without a glycoprotein IIb-IIIa receptor inhibitor) has been approved for facilitated PCI. GPIIb/IIIa inhibitors should be considered in patients with symptoms refractory (persistent chest pain or ECG changes consistent with ischemia) to standard therapy. Otherwise these agents may be given at the time of angiography. Based on REPLACE-2 study, a reasonable alternative to heparin is to use bivalirudin for patients who will be undergoing percutaneous coronary interventions.

Current ACC guidelines recommend treating the culprit vessel when feasible and deferring surgical or PCI-based revascularization of other vessels until the patient has stabilized and the clinically most appropriate strategy determined.

Evidence supporting this recommendation is of classes: C, R

# 48. Cardiac Care Unit (CCU) Admission

Patients who present with acute ST-segment elevation, hemodynamic instability, or both should be admitted to the CCU. Early use of adjunctive medications can be reconsidered. Once the issue of surgery is clarified, consider the early use of clopidogrel (Plavix®) for those in whom PCI is planned. (See Emergency Interventions Algorithm Annotations #20 to #31.) A CCU admission order set template has been developed by the ICSI acute coronary syndrome work group and is available from ICSI -- see the "Support for Implementation" section of the original guideline document.

49. CCU Care: Chronic Adjunctive Medications/Phase I Cardiac Rehabilitation

A protocol should be in place to guide routine orders for continuous monitoring, oxygen delivery, IV therapy, activity, laboratory and diagnostic tests, diet, and medications.

Use of the following medications should be considered:

- ASA/aspirin\* should be continued as the clinical situation warrants.
   ASA/aspirin has been shown to reduce reinfarction and mortality long-term, and should be continued whenever possible. Use of non-steroidal anti-inflammatory drugs (NSAIDs) and COX-2 inhibitors may reduce the cardioprotective benefits of aspirin.
- Clopidogrel\*\* ASA/aspirin (dose should be 81 mg when given with clopidogrel) with clopidogrel in intermediate and high-risk ACS patients is beneficial. Anyone with an allergy to aspirin or NSAIDs should receive a bolus dose of clopidogrel (300 mg) with maintenance dosing indefinitely. For patients who present with unstable angina or non-ST elevation MI who are not at high risk for bleeding, clopidogrel should be continued for 9–12 months. For patients undergoing a non-coated stent, clopidogrel should be continued for at least one month. For patients who receive a sirolimus eluting stent, clopidogrel should be continued for at least three months, and at least six months for a paclitaxel eluting stent. For patients who have undergone brachytherapy, clopidogrel should be continued for 12 months. ASA/aspirin plus clopidogrel or clopidogrel alone can also be used with patients who have stents. If clopidogrel is given and coronary artery bypass surgery planned, clopidogrel should be held for five days prior to surgery due to increased risk of perioperative bleeding.
- Beta-Blockers\* Beta-blockers reduce mortality, readmission, and reinfarction for both CAD and CHF. They should be instituted and/or continued whenever possible. Intravenous esmolol should be considered if a clinician is concerned about potential adverse effects of beta-blockers. Patients who prove intolerant of a beta-blocker after a large infarction should be reconsidered for beta-blocker therapy after discharge.
- ACE inhibitors\* ACE inhibitors (ACEI) are indicated (angiotensin receptor blockers [ARBs] if ACEI aren't tolerated; in addition to beta-blockers, when possible) for most patients following AMI to reduce mortality and morbidity associated with large infarcts with significant left ventricular (LV) dysfunction, reduce adverse ventricular remodeling that may result in further reduction in ejection fraction (EF), and for potential reduction of future MI and stroke. Consider hydralazine/isosorbide dinitrate if intolerant to ACEIs or ARBs or either drug is contraindicated.

Evidence supporting this recommendation is of class: A

 Calcium channel blockers may be useful for control of blood pressure and ischemic pain when beta-blockers are contraindicated but

<sup>\*</sup>Shown in large clinical trials to reduce infarction mortality in all MIs.

<sup>\*\*</sup>Shown in large clinical trials to reduce infarction mortality in non-STEMIs.

- should be avoided in patients with decreased LV function or heart failure. The short-acting dihydropyridine calcium channel blockers (e.g., nifedipine) may be associated with increased risk and should be avoided in acute ischemic syndromes.
- Oral nitrates may benefit selected patients with postinfarction angina or CHF.
- Low-molecular-weight heparin has been shown to be superior to unfractionated heparin in patients without ST-segment elevation and can preferentially be used in subcutaneous dosing (e.g., enoxaparin sodium [Lovenox®], 1 mg/kg every 12 hours). Heparin may be continued for 2 to 4 days or maintained until conversion to warfarin is completed. If unfractionated heparin is used, the dose should be regulated to maintain an activated partial thromboplastin time of 50 to 75 seconds.
- Warfarin therapy may be initiated in certain clinical situations (e.g., postinfarction CHF or anterior MI with high risk of LV thrombus) as soon as clinical stability is achieved and invasive diagnostic studies are completed. The usual target international normalized ratio is 2.0 to 3.0.
- Oral antiarrhythmics are not recommended, especially when LV function is reduced. Flecainide acetate (Tambocor®) and sotalol hydrochloride (Betapace®) should be avoided in patients with significant structural heart disease unless clearly indicated on the basis of electrophysiologic study for the suppression of life-threatening ventricular arrhythmias. Beta-blockers are the current drug of choice when tolerated. Routine use of amiodarone hydrochloride (Cordarone®) in post-MI patients with nonsustained ventricular ectopy has not been shown to reduce mortality.

### Evidence supporting this recommendation is of classes: A, M

- Statins. The large majority of patients who have an AMI have high serum lipid levels. Lipid treatment, including administration of statins, should be addressed as soon as possible. A patient's lipid status should be determined within the first 24 hours. If the low-density lipoprotein (LDL) level is greater than 70 mg/dL, the patient should be started on a statin within the first 24 hours of the onset of MI.
- Tobacco cessation should be addressed as soon as possible for patients who smoke or use tobacco products. Appropriate treatment may include administration of bupropion and/or a nicotine patch in the hospital.
- Glycemic control. Tight control of blood glucose in patients with diabetes is recommended.

Medication tables and dosing protocols are attached in Appendix B, "AMI Acute Medications and Adjunctive Therapy" in the original guideline document.

#### Phase 1 Cardiac Rehabilitation

With shortened length of stay, teachable moments may be limited. As a result, timely initiation of education on lifestyle modification is crucial. Phase

1 cardiac rehabilitation should begin as soon as the patient is stable and painfree. Goals are to minimize harmful effects of immobilization, assess the hemodynamic response to exercise, manage the psychosocial issues of cardiac disease, and educate the patient and family about lifestyle modification including:

- Tobacco cessation
- Dietary instruction including a heart healthy diet
- Manageable exercise regimen should be explained.

# 50. Complications?

Arrhythmic complications include sinus bradycardia, Möbitz I block (Wenkebach), Möbitz II block, complete heart block or asystole, premature ventricular contractions (PVCs), ventricular tachycardia, ventricular fibrillation, accelerated idioventricular rhythm, and supraventricular arrhythmias (atrial flutter, atrial fibrillation, and supraventricular tachycardia). Ischemic complications include postinfarction angina. Mechanical complications include papillary muscle dysfunction, rupture with significant mitral regurgitation, ventricular septal rupture, myocardial rupture, right ventricular infarction, pericarditis with or without tamponade, LV dysfunction, and aneurysm formation.

Evidence supporting this recommendation is of classes: C, M

## 52. Transfer to Post-CCU Care

Patients should be transferred from the CCU to the telemetry or step-down unit when they are pain-free, hemodynamically stable, and meet the institution's protocol for admission to the telemetry unit (usually 12 to 24 hours after MI). Discontinuation of cardiac monitoring should be considered for patients who attain electrical stability (usually within 3 days of infarction).

#### 54. Risk Stratification

Assessment of ejection fraction is important in predicting prognosis. Most patients should undergo echocardiography or other assessment of LV ejection fraction. A treadmill test is useful for assessing functional reserve but is not useful for predicting recurrence of AMI. If ST-segment depression or angina is present early in treatment, angiography should be considered. If the patient is unable to exercise, pharmacologic stress testing should be considered, and if the ECG is uninterpretable, stress imaging (nuclear or echocardiographic) should be considered.

Patient with no high-risk indications following thrombolytics therapy may be stratified non-invasively into low, medium, and high risk.

Some clinicians may elect to measure multiple cardiac biomarkers in patients with myocardial infarction. This may especially be helpful in those in whom risk stratification is not available by other clinical evidence. The work by Sabatine, Morrow et al demonstrated the utility of cardiac troponins, c-

reactive protein and B type natriuretic peptide measurements (BNP). This work demonstrated that patients with elevations of all three cardiac biomarkers had significantly higher risks of recurrent MI and death than those with only two or one elevated. There was a progressive step-wise increase in risk going from one abnormality to two abnormalities to elevations of all three biomarkers. For patients with obvious clinical heart failure there is little utility in measuring BNP during hospitalization for AMI. At present, there is no clear consensus about what to do with an elevated BNP value during hospitalization for AMI. Some have suggested there is limited utility in measuring BNP in patients if one is planning an intentional invasive strategy as well. Some have suggested that a lack of BNP elevation may identify patients hospitalized for AMI who are eligible for early discharge strategies. Further studies are warranted to fully understand how to apply BNP values in these populations. The most prudent strategy may be to not measure BNP in the great majority of patients until further data are available.

Evidence supporting this recommendation is of class: R

#### 55. Patient at Increased Risk and Needs Intervention?

Patients who are at increased risk for adverse prognosis after AMI and who are also candidates for short-term intervention include those with a large amount of myocardial necrosis (ejection fraction less than 40%), residual ischemia (angina during hospitalization or exercise testing), electrical instability (greater than 10 PVC/hr), left main or three-vessel CAD, limited exercise tolerance, or rales/crackles in more than one-third of lung fields.

The following factors increase long-term risk:

- 70 years of age or older
- Previous infarction
- Anterior-wall MI
- Hypotension and sinus tachycardia
- Diabetes
- Female gender
- Continued smoking
- Atrial fibrillation
- Heart failure

Patients able to exercise more than four metabolic equivalents (METs) had less than a 2% subsequent incidence of death or myocardial infarction within one year compared with 18% for those in the high-risk group.

Evidence supporting this recommendation is of class: B

## 56. Cardiac Catheterization

Angiography should be performed in patients at increased risk as defined in Emergency Intervention Algorithm Annotation #27, "Risk Assessment (ACC/AHA Criteria)."

Recent trials (collectively FRISC II and TACTICS-TIMI 18) suggest an early aggressive/invasive approach (early diagnostic coronary angiography and appropriate PCI or CABG) within 48 hours of presentation, in non-ST ACS (with ST segment deviation, elevated cardiac markers or TIMI Risk Score greater than 3), significantly reduces the risk of major cardiac events. However, the majority of non-STEMI patients should undergo coronary angiography.

#### 57. Revascularization Candidate?

CABG should be considered in patients with left main, three-vessel or two-vessel disease with left anterior descending coronary artery involvement and demonstration of ischemia or in patients who would not receive the ideal benefit from PCI. Pharmacologic or stress test imaging may be helpful if myocardial viability is uncertain and revascularization is considered.

PCI should be considered for patients with acceptable anatomy in whom its prognostic effect has been most clearly demonstrated: significant residual ischemia, CABG candidacy, and failure of maximal medical therapy (two of three medications) to control angina or contraindications to medications.

# 60. Continue Adjunctive Medications

See STEMI Algorithm Annotation #49, "CCU Care: Chronic Adjunctive Medications/Phase I Cardiac Rehabilitation" above.

## 61. Secondary Prevention and Risk Factor Modification

Modification of risk factors (e.g., high lipid levels, hypertension, smoking) significantly reduces subsequent cardiovascular mortality. Risk factor counseling must be documented in the medical record in a consistent manner. A "care plan" or "critical pathway" approach with flow sheets may be used. Ongoing patient monitoring and feedback are important. Adjunctive therapy (ASA or clopidogrel if ASA allergic, beta-blockers, warfarin for large anterior infarctions, ACE inhibitors, and statins) should be continued.

Efforts targeted at exercise (as an adjunct, in the management of other risk factors), lipid management, hypertension control, and smoking cessation can reduce cardiovascular mortality, improve functional capacity, attenuate myocardial ischemia, retard the progression and foster the reversal of coronary atherosclerosis, and reduce the risk of further coronary events.

The Cooperative Cardiovascular Project (CCP) has documented a discrepancy between risk factor counseling documentation and actual practice during hospital stays of patients with MI. Therefore, documentation of smoking cessation counseling has become one of 13 indicators judged to be representative of quality care by the CCP steering committee.

- 1. Smoking cessation is clearly linked to mortality and morbidity after MI.
- 2. Aggressive treatment of dyslipidemia can reduce subsequent myocardial ischemia.

- 3. Hypertension control will reduce recurrent cardiac events.
- 4. Exercise alone is only modestly effective for secondary prevention.
- 5. A case management system may be more effective than usual care in long-lasting risk factor modification.

Teaching must be done when the patient is ready, and ideally is based on patient-\*derived learning priorities. Teaching moments may be best taken advantage of by a team approach involving physician and nursing staff during the hospital stay. Ongoing outpatient follow-up and progress feedback are important for patient adherence.

Evidence supporting this recommendation is of classes: A, D, M, R

# 62. Discharge

Complete and document the following before discharge:

- Patient education that includes discharge diagnosis, medical regimen, lifestyle modification issues, and functional limitation (including resumption of sexual activity and driving)
- Scheduling of a follow-up appointment with the primary care physician
- Targeting a return-to-work date. Patients with sedentary jobs often return to work in 2 to 3 weeks. More physically demanding jobs often can be resumed in 4 to 6 weeks unless significant ischemia is present.

Patients are commonly discharged in less than three days following successful primary PCI with evidence of complete or near complete salvage of threatened myocardium. Though patients should avoid strenuous exertion for several weeks during the stent healing phase, many such patients may return to sedentary or only moderately active work activities within days of discharge.

Most patients with uncomplicated MIs should be discharged within five days. Patients undergoing primary PCI who are at low risk with an uncomplicated course may be discharged on the third day. Early reperfusion and definitive angiography revealing little or no residual injury or disease has increasingly demonstrated improved myocardial salvage and enhanced patient stability. Discharge may be individualized according to the degree of salvage and stability. In many centers some patients are safely discharged within 24 hours when salvage is nearly complete.

Information on discharge medication is attached in Appendix C, "Medications to Consider on Discharge" in the original guideline document.

Evidence supporting this recommendation is of class: A

### 63. ECG-Monitored Exercise Needed?

Most patients do not require an ECG-monitored, hospital-based (phase 2; outpatient) exercise program, but those with any of the following characteristics may be at increased risk for infarction or sudden death with

unmonitored exercise and should be considered for a phase 2 program, usually lasting 1–4 weeks: very low functional capacity (less than 4 METs), severely depressed ventricular function (ejection fraction less than or equal to 35%), complex resting ventricular arrhythmias, exercise-induced hypotension, exertional angina or significant silent ischemia, or inability to initiate a self-directed exercise program.

For certain patients, referral to a phase 2 program may facilitate earlier hospital discharge by providing emotional support in the outpatient hospital setting. The decision to refer a patient to a phase 2 program should be made on a case-by-case basis. The patient's current exercise capacity and the demands of expected occupational and recreational activities should be considered.

Most patients with uncomplicated MIs achieve a return to their prehospital levels of activity without a formal monitored exercise program. Home exercise training programs have been shown to be beneficial in certain low-risk patient groups.

Certain patients felt to be at higher risk of complications post discharge are more likely to require monitoring during exercise in the immediate post discharge period.

Evidence supporting this recommendation is of classes: A, M, R

#### 64. Phase 2 Cardiac Rehabilitation - Outpatient

Patients at increased risk for adverse events during exercise should be considered for phase 2 cardiac rehabilitation. The length of time spent in phase 2 should be dependent on improvement in functional capacity. Phase 2 (outpatient monitored) programs, if indicated, consist of medically supervised exercise with continuous ECG monitoring attended by trained personnel who have emergency equipment. Most phase 2 programs are hospital-based. Health education and risk factor modifications need to be included in these programs.

More patients should be enrolled in a Phase 2, monitored exercise program. In the past, the main emphasis was exercise-based, but today the focus also includes risk factor modification, education, and counseling.

Research shows that a cardiac rehabilitation program based on regular exercise and education focused on risk factor reduction is both efficient and effective in altering the course of coronary heart disease.

Cardiac rehabilitation programs have been shown to decrease mortality but have no effect on nonfatal recurrent myocardial infarctions. Unless there is a long-term effort of encouragement, most patients will revert back to previous sedentary activities.

This initial outpatient phase includes comprehensive evaluation, education, and treatment for outpatients who have experienced a cardiac-related event.

Phase 2 patients are monitored with continuous ECG, blood pressure, heart rate and subjective RPE ratings.

## Goals of Phase 2 Rehab:

- Assist with appropriate risk factor modification
  - Smoking cessation
  - Lipid management and low fat diet
  - Stress management and relaxation techniques
  - Weight loss and BMI measurement
  - Safe exercise guidelines
  - Blood pressure control
  - Diabetes education and glucose monitoring
- Increase exercise tolerance and endurance to enable patient to perform activities of daily living, and return to, or above previous level of function
- Improve quality of life
- Improve psychological well-being and provide emotional support
- Provide educational support and resources

## **Education Topics:**

- Anatomy and physiology of the heart
- Nutrition
- Heart disease risk factors and modification
- Stress reduction
- Emotional aspects of heart disease
- Cardiac medications
- Aerobic exercise and exercise progression
- Cardiac signs and symptoms

#### Exercise Prescription

An exercise prescription consists of:

- Intensity of exercise: In general, moderate intensity (to 40–60% of functional capacity) is advisable during the first weeks of conditioning with a goal to reach 40–85%, or that of the functional capacity of the population at large.
- Monitoring rate of perceived exertion (RPE) is very useful. This is advantageous for many reasons: it is unaffected by negative chronotropic medications unlike heart rate monitoring; it is quite reproducible across age, gender, and cultural origin; and lastly, it only requires patient attunement to symptoms
- Monitoring METs: Monitoring is determined by the patient's post-MI exercise tolerance test and/or in rehab is highly individual. The table in Appendix D of the original guideline document can be used to compare the demands of certain activities to the patient's known capacity. However, its usefulness lies primarily in vocational counseling.

Refer to the original guideline document for more information on exercise prescription including exercise heart rate, exercise tolerance, mode, frequency, intensity, duration, and progression.

Evidence supporting this recommendation is of classes: A, R

#### 65. Phase 3 Cardiac Rehabilitation

Phase 3 is a maintenance program based on the continuation of a heart healthy lifestyle. The program is designed for patients who have completed a Phase 2 cardiac rehabilitation program or for individuals with a cardiac history or significant cardiac risk factors. Patients are not continually monitored by ECG, but spot check ECGs and daily blood pressures and heart rates are recorded. Trained staff continues to provide support and education for risk factor modification and exercise progression. Warm up, aerobic exercise, stretching, and strength training (when appropriate) are included in Phase 3.

Evidence supporting this recommendation is of classes: A, M, R

66. Short-Term Follow-Up: Chronic Adjunctive Medication/Outpatient Management

Chronic Adjunctive Medications

Use of enteric-coated ASA/aspirin or ASA/aspirin plus clopidogrel should be continued. Use of beta-blockers following MI has been shown to reduce ischemia, prevent arrhythmias and reinfarction, and improve survival. Patients with large anterior infarctions may benefit from therapeutic warfarin therapy (INR 2-3), usually for 3 months to reduce risk of systemic emboli. ACE inhibitors provide long-term cardiac protection for patients (with or without symptoms) with left ventricular ejection fraction (EF) of less than 40%.

Most patients should be receiving a statin or alternative lipid-lowering medication at discharge from the hospital. Lipid-lowering therapy should be considered for patients who have undergone PCI or CABG and patients whose low-density lipoprotein cholesterol level is 100 mg/dL or greater. Calcium channel blockers should be considered only for patients with NSTEMI who cannot take beta-blockers and patients without CHF or decreased LV ejection fraction. Oral nitrates should be considered for patients with ongoing ischemia.

Clinicians should be measuring LDL cholesterol and C-reactive protein levels in patients following myocardial infarction. Recent evidence has revealed that use of statin therapy following hospitalization for AMI reduces long-term risks. A sub-study from the PROVE-IT trial has demonstrated that the achievement of an LDL less than 70 and C-reactive protein (CRP) less than 2 mg/l around 30 days following hospitalization was associated with the lowest risk of recurrent clinical events by two years of follow-up. The achievement of these goals was more important than the selection of an individual statin agent. This evidence supports the measurement of LDL cholesterol and C-reactive

protein levels about one month following hospital discharge and the aggressive use of statin therapy to achieve an LDL less than 70 mg/dl and a CRP of less than 2 mg/l by that time frame. Some patients may achieve these values through moderate statin doses, most will require higher doses of potent statins, and some patients will require combination therapy with a statin plus ezetimibe. Of interest, achievement of either goal alone (LDL less than 70 or CRP less than 2) but not both was associated with significantly higher recurrence risks.

## Follow-Up Visits

Usually, patients should return for a follow-up visit with their cardiologist or primary care physician within 2 to 3 weeks so the physician can monitor progress, answer questions, and consider further risk stratification (i.e., stress testing). Risk factor modification should be continued.

## Phase 4 Cardiac Rehabilitation

Phase 4 cardiac rehabilitation begins after the desired functional capacity has been attained (usually greater than or equal to 8 METs) and/or  $VO_2$ max has reached a plateau. Maintenance is the principal goal. The exercise prescription should continue as at the end of phase 3 unless angina or exercise intolerance develops, either of which requires cessation of exercise and urgent medical attention. Refer to METs table in Appendix D and "Nomogram of the prognostic Relations Embodied in the Treadmill Score" in Appendix E of the original guideline document for guidance on setting exercise goals.

#### AMI Complications Algorithm Annotations

## 68. Arrhythmic Complication(s)?

Arrhythmic complications including sinus bradycardia, Möbitz I (Wenkebach), PVCs, accelerated idioventricular rhythm, and supraventricular arrhythmias (transient atrial flutter, atrial fibrillation, supraventricular tachycardia, and hemodynamic stability) are generally benign and will usually require symptomatic therapy. Transient Mobitz II block with MI may be treated symptomatically. Permanent pacing is indicated for persistent and symptomatic second and third degree AV block.

Six Centers for Medicare and Medicaid Services (CMS) covered indications for defibrillators:

- 1. Documented episode of cardiac arrest due to ventricular fibrillation (VF), not due to transient or reversible cause
- 2. Documented sustained ventricular tachyarrhythmia (VT) either spontaneous or induced by an electrophysiologic (EP) study, not associated with an AMI and not due to transient or reversible cause
- Documented familial or inherited conditions with a high risk of life threatening VT such as long QT syndrome or hypertrophic cardiomyopathy

- 4. Coronary artery disease with documented prior MI, ejection fraction (EF) less than 35%, an inducible sustained VT, or VT at EP study
- 5. Documented prior MI, EF less than or equal to 30%, QRS duration of greater than 120 msec (patient must not have Class IV heart failure, shock, CABG, PCI, MI within three months or a need for coronary revascularization or predicted survival less than one year).
- 6. Patients with dilated cardiomyopathy, documented prior MI, heart failure, and left ventricular EF less than or equal to 35% for longer than nine months.

# 69. Treat Arrhythmic Complication(s)

# Key Points:

• ACLS quidelines provide in-depth descriptions of short-term treatment.

Refer to the original guideline document for more information on treatment of arrhythmic complications, including atrioventricular/bundle branch blocks, ventricular arrhythmias, accelerated idioventricular rhythm, and supraventricular arrhythmias.

Evidence supporting this recommendation is of classes: B, C

# 70. I schemic Complication(s)?

Ischemic complications include postinfarction angina.

# 71. Treat I schemic Complication(s)

Treatment of postinfarction angina should be correlated with ECG changes, if possible. Optimal therapy consists of beta-blockers and long-acting nitrates. If beta-blockers are not tolerated or are ineffective and LV function is not significantly depressed, a calcium channel blocker may be used. Early coronary angiography should be considered. Angina after MI may be confused with pericarditis. Aneurysm formation should be a consideration.

## 72. Mechanical Complication(s)?

Mechanical complications may include papillary muscle dysfunction or rupture with significant mitral regurgitation, ventricular septal rupture, myocardial rupture, right ventricular infarction, pericarditis with or without tamponade, LV dysfunction, and aneurysm formation.

# 73. Treat Mechanical Complication(s)

Papillary muscle dysfunction is evidenced by the murmur of mitral regurgitation, typically within five days of infarction.

Papillary muscle rupture may occur within 10 days of the event. Findings include development of sudden CHF or pulmonary edema, often but not always accompanied by a new holosystolic apical murmur. Diagnosis is

verified by echocardiography. Stabilization is achieved by one or more of the following: aggressive use of diuretics and vasodilators, insertion of a Swan-Ganz catheter, insertion of an intraaortic balloon pump (IABP). Because of the high mortality rate with this complication, urgent surgical repair is indicated.

Ventricular septal rupture (VSR) occurs within 1 week of infarction and results in left-to-right shunting and subsequent hemodynamic deterioration. VSR is suggested by the presence of a new, harsh, holosystolic murmur that is loudest along the lower left sternal border; this may be accompanied by a thrill. Patients may also have symptoms of right-sided heart failure with right ventricular (RV) PO<sub>2</sub> step-up and may have less pulmonary congestion than patients with papillary muscle rupture. The diagnosis is confirmed by two-dimensional echocardiography. Patients are best stabilized by vasodilator therapy, insertion of a Swan-Ganz catheter or an IABP, or all of these. Because of the high mortality rate, urgent surgical repair is indicated.

Myocardial rupture is a common cause of sudden death after AMI. Symptoms or findings include emesis, persistent restlessness, anxiety, and persistent ST-wave elevation on ECG. Rupture usually occurs within 5–7 days of MI. LV free-wall rupture leads to hemopericardium and subsequent death from tamponade. Contained rupture may result in formation of a pseudoaneurysm. Surgical resection is recommended.

Right ventricular (RV) infarction is suspected in patients with inferior infarction complicated by low cardiac output, hypotension, oliguria, jugular venous distention, and clear lung fields without radiographic evidence of pulmonary venous congestion. Infarction can be confirmed by ECG findings (ST-segment elevation in right precordial leads V<sub>4</sub>R through V<sub>6</sub>R in the presence of inferior ST elevation), two-dimensional echocardiography, or pulmonary artery catheter demonstrating a disproportionate elevation of right atrial pressure compared with pulmonary capillary wedge pressure. Treatment consists of intravascular volume expansion and use of inotropic agents; if the patient loses sinus rhythm, temporary pacing to re-establish AV synchrony should be considered. Agents that reduce RV preload, such as nitroglycerin, diuretics, and large doses of morphine, should be avoided. ACE inhibitors and beta-blockers may require dose reduction or discontinuation with milder presentation of RV dysfunction post-MI.

Post-MI pericarditis can be early (occurring within 72 to 96 hours after AMI) or occasionally delayed (typically occurring weeks after MI); the latter is called Dressler's Syndrome. Early pericarditis is suspected in patients with pericardial friction rub, usually heard on the second or third day after AMI, and chest pain that may extend to the back, neck, or shoulders that is intensified by movement and respiration and relieved by sitting up or leaning forward. Treatment consists of anti-inflammatory agents and reassurance. Echocardiography to assess for possible incomplete myocardial rupture should be considered. It is important to emphasize to the patient that the recurrent pain is not the result of recurrent infarction. Risk of hemopericardium is increased in patients receiving anticoagulants; development of a pericardial effusion can be detected by close clinical observation and echocardiography.

Dressler's Syndrome is characterized by an increase in erythrocyte sedimentation rate, leukocytosis, and more frequent pleural and pericardial effusions than in early pericarditis. The Incidence of Dressler's Syndrome is roughly 1 to 3 % of AMI patients. Because of the increased incidence of pericardial effusion, anticoagulation should be used with caution. Treatment for pericardial effusion with impending tamponade is pericardiocentesis, preferably guided by echocardiography.

Risk of developing LV dysfunction and subsequent HF is greatly increased in patients with more extensive MI. Restricted diastolic filling patterns on echocardiography may predict subsequent clinical HF.

Refer to the original guideline document for more information.

Evidence supporting this recommendation is of classes: A, B, C, D, R

# Special Work-Up Algorithm Annotations

- 77. Clinical Features Suggest Dissecting or Symptomatic Aneurysm?
  - Clinical findings of ischemia involving several organ systems
  - Pain typically "tearing" or "ripping"
  - Pain radiation from chest to back, hips and lower extremities
  - Common findings: hypertension, cardiac murmurs, systolic bruits, diminished or absent pulses
  - Chest x-rays (CXR) abnormalities around aortic knob, increased diameter of ascending aorta
  - Blood pressure discrepancy between right and left arm
- 78. Diagnosis of Dissection, Immediate Computed Tomography (CT)
  Angiogram or Echo/Transesophageal Echocardiography (TEE);
  Magnetic Resonance Imaging (MRI) if Clinically Stable and Patient
  Asymptomatic
  - CT angiogram is generally the quickest and most readily available diagnostic test.
  - TEE with a biplane probe is equally diagnostic and preferable in patients with renal insufficiency or allergy to contrast dye.
  - MRI remains the most accurate test, but requires a stable patient. MRI should be avoided if a type A dissection is suspected.

Evidence supporting this recommendation is of classes: C, R

79. Test Diagnostic of Type A Dissection or Symptomatic Aneurysm?

The imaging procedure should establish the presence or absence of an aneurysm and the presence or absence, and location, of a dissection.

- 80. Arrange for Immediate Cardiovascular Surgery Consultation/Nitroprusside + Esmolol Drip
  - Surgical intervention for symptomatic thoracic aneurysms and proximal (type A; ascending aorta) dissections
  - Control blood pressure (BP) with nitroprusside or esmolol drip

# Evidence supporting this recommendation is of class: R

#### 81. Treatment of Distal Dissection

- Distal (type B; distal to left subclavian artery) aortic dissections generally appropriate for pharmacologic therapy
  - Nitroprusside or esmolol drip to control BP and heart rate (eliminate pain and stabilize dissection)
  - Consider surgery if therapy not effective

# 82. Symptoms, ABGs (Arterial Blood Gases), CXR (Chest X-Ray) Suggest Pulmonary Embolus?

- Symptoms may include dyspnea, tachypnea, pleuritic chest pain
- Physical findings extremely variable, may include fever, wheezing
- ECG non-specific ST-T changes
- CXR normal, pleural effusion, wedge-shaped infiltrate
- ABG abnormal A-a gradient

# 84. Symptoms, ABGs, CXR Suggest Pneumothorax?

- Idiopathic or spontaneous pneumothorax sudden onset of pleuritic chest pain and dyspnea (pleuritic pain more prominent with small pneumothorax, dyspnea with large)
- ABGs may be abnormal

## 85. Consider Chest Tube and Hospitalization

- Pneumothorax greater than 10 to 20% usually require chest tube
  - Primary pneumothorax occurs in otherwise healthy people (idiopathic most frequently in tall young males, catamenial associated with endometriosis and menses)
  - Secondary pneumothorax chronic obstructive pulmonary disease (COPD), asthma, pneumonia, cystic fibrosis
- Outpatient treatment possible if progression unlikely and patient reliable
  - Catheter aspiration followed by several hours of observation
  - Indwelling catheter attached to Heimlich valve
- Inpatient treatment if pneumothorax is secondary or significant symptoms
- Reabsorption slow 1.25% per day

# 86. Symptoms, Signs Suggest Pericardial Disease?

- Chest pain worsened with inspiration, coughing, position changes or swallowing
- Pericardial friction rub
- ECG ST-T changes
- Etiology infectious, neoplastic, metabolic, inflammatory autoimmune disorders, post-MI (Dressler's syndrome)
- Drug related hydralazine, procainamide, isoniazid, phenytoin, doxorubicin
- Consider blunt trauma, post-op

## 87. Tamponade?

• Chest pressure and shortness of breath

- Exam elevated jugular venous pressure, hypotension, tachypnea, narrow pulse pressure, pulsus paradoxus greater than 20 mmHg
- ECG may reveal electrical alternans
- CXR normal or enlarged cardiac silhouette
- Echocardiogram diagnostic test of choice
- Pericardial space typically contains 50cc of fluid, with chronic accumulation may contain up to 2,000cc
- With acute, rapid accumulation, overt tamponade may develop with as little as 150cc

# 88. Pericardiocentesis - Prefer Echocardiography (ECHO) Directed

- Echo-directed apical pericardiocentesis procedure of choice
- Subxyphoid approach if echo not available and patient unstable

#### 89. Admit to CCU/Monitored Bed

The patient should be observed in a CCU/monitored bed setting.

## 90. Echo; Discharge?/Consider Treatment

- Pericarditis without tamponade -- obtain echocardiogram
- Nonsteroidal anti-inflammatory drugs (NSAIDs) or ASA and close follow-up for viral or idiopathic

# Non-Cardiac Causes Algorithm Annotations

# 92. Symptoms, Signs, CXR Suggest Pleural or Parenchymal Pulmonary Disease?

Patients with pulmonary or pleural disease frequently have a presenting complaint of chest pain with or without shortness of breath. A detailed history, physical examination, ECG, chest x-ray and laboratory evaluation typically will often suggest the diagnosis. Differential diagnoses include chronic obstructive pulmonary disease (COPD), asthma, infectious processes, and malignancies. Specific management of these diagnoses is beyond the scope of this guideline.

#### 93. Evaluate for Observation or Admission

Disposition decisions are largely dependent on the patient's stability. The initial treatment must be directed toward treating any instability and searching for the etiology of the symptoms. Pulse, blood pressure, respirations, and level of consciousness must be assessed. Other factors that need to be considered are age, general state of health and immunocompetency, and reliability. If a patient is labile or unstable, or at risk of becoming unstable, admit the patient.

## 94. Symptoms and Signs Suggest Chest Wall/Costochondritis?

Costochondritis and intercostal strain frequently presents with chest pain. Typically, the patient is able to localize the discomfort to a fairly limited area.

Physical examination should reveal reproducible pain at the site of the discomfort.

# 95. NSAI Ds/Thermal Application/Follow-Up as needed (PRN)

Once the clinician has determined that the chest discomfort is limited to the chest wall, treatment with nonsteroidal anti-inflammatory medication should be started and the patient should be advised on local application. Follow-up may be arranged as needed. For expanded discussion, refer to the National Guideline Clearinghouse (NGC) summary of the Institute for Clinical Systems Improvement (ICSI) guideline <u>Assessment and Management of Acute Pain</u>.

Evidence supporting this recommendation is of classes: C, R

# 96. Consider Gastrointestinal (GI) Diagnosis?

GI disorders are sometimes perceived by the patient as chest pain. Once the clinician is confident that no intra-thoracic processes are the cause of the discomfort, a GI diagnosis should be considered.

#### 97. Gastrointestinal Evaluation

Commonly history, physical examination, and a laboratory evaluation will suggest a GI diagnosis. Further evaluation of this is beyond the scope of this guideline.

### 98. Reconsider Differential Diagnosis

If the clinician, after initial evaluation and work-up, does not arrive at a likely working diagnosis, he/she may have to go back and reconsider the entire differential diagnosis a second time in order to make certain that no serious condition has been missed. The clinician may then have to redirect his/her search for a diagnosis to conditions of the thoracic spine and thoracic nerves. Other considerations are somatization and anxiety disorders. These may be more or less obvious after careful consideration. For anxiety diagnoses, refer to the NGC summary of the ICSI guideline <a href="Major Depression in Adults in Primary Care">Major Depression in Adults in Primary Care</a>.

Differential diagnoses of thoracic spine and thoracic neuralgias include metastatic malignancy, multiple myeloma, arthritic processes, ankylosing spondylitis, osteomyelitis, kyphoscoliosis, and herpes zoster.

Atypical chest pain associated with mitral valve prolapse is a poorly understood symptom.

## Clinic Evaluation Algorithm Annotations

100. Initial Focused Assessment for High-Risk History, Physical Exam, and Other Findings

History should include characterization of pain, exacerbating or relieving factors, associated symptoms, and risk factors for coronary disease. Physical exam should include careful cardiovascular and pulmonary exam, peripheral vascular exam, and evaluation for hypertension and hypercholesterolemia. Lab studies may include resting ECG, chest x-ray, hemoglobin, and others if clinically indicated.

The patient's description of pain and the history of previous coronary disease are by far the most important parts of the history.

Carotid bruits, peripheral vascular disease, and xanthomas on physical exam suggest a higher likelihood of coronary disease. The resting ECG may show evidence of previous infarction.

Direct provider education toward completing the history evaluation.

High-risk symptoms on initial presentation include:

### History

- Severe or ongoing pain
- Pain lasting 20 minutes or more
- New pain at rest or with minimal activity
- Severe dyspnea
- Loss of consciousness

# Physical Findings

- Hypotension or other signs of underperfusion
- Tachycardia or bradycardia
- Pulmonary edema, cyanosis

## **ECG Findings**

- ST elevation greater than 1 mm on two contiguous leads suggesting AMI
- New ST or T wave changes
- ST depression greater than 1 mm at rest
- New LBBB

Evidence supporting this recommendation is of class: C

# 102. Initiate Emergency Interventions and Transfer to ED as Appropriate

Initiate emergency intervention as appropriate and transfer the patient as soon as possible for further emergency intervention.

A patient complaining of chest pain should immediately be placed on a cardiac monitor. Vital signs should be taken, IV started, oxygen administered, and immediate ECG taken. Institution of stabilizing therapy (including

nitroglycerin (NTG) and chewable aspirin for suspect anginal pain) prior to the completion of the history or physical is appropriate and often necessary at this level.

## 103. CAD Diagnosis Secure?

When the clinical setting and history suggest typical angina pectoris (substernal pain provoked by exertion and relieved by nitroglycerin or rest), the physician is very likely correct in assuming an ischemic coronary syndrome. Treatment and prognostic evaluation may proceed as outlined in the NGC summary of the ICSI guideline <a href="Stable Coronary Artery Disease">Stable Coronary Artery Disease</a>.

# 104. Refer to the NGC summary of the ICSI guideline <u>Stable</u> <u>Coronary Artery Disease</u>

Typical angina pectoris, if stable for 60 days and without evidence of recent myocardial infarction, may be treated under the NGC summary of the ICSI guideline Stable Coronary Artery Disease.

#### 105. Ischemic Heart Pain Possible?

When coronary disease is of intermediate probability, a stress test may contribute supplemental information. When coronary disease is unlikely based on highly atypical symptoms and low prevalence of coronary disease among the population to which the patient belongs, stress testing may be misleading.

# 106. Choose Stress Test/Cardiology Referral Optional

Choose the best type of cardiac stress test based on:

- The resting cardiogram
- The patient's ability to walk
- Local expertise

### 107. Can Patient Walk?

In patients who cannot exercise, consider pharmacologic stress and imaging test (with adenosine, dipyridamole, or dobutamine). Physical exercise is the most physiologic form of cardiovascular stress. If one doubts how far a patient will be able to walk, it might still be worthwhile to attempt treadmill exercise. The occasional patient with orthopedic restriction may be able to perform bicycle ergometry.

# 109. Resting ECG Interpretable?

Marked resting ECG abnormalities, such as LBBB, LVH with repolarization abnormality, ventricular pre-excitation, or ventricular paced rhythm, render the exercise ECG uninterpretable for ischemic changes. Patients on digoxin and those with less than 1 mm resting ST depression may undergo standard ECG stress testing, provided the clinician realizes that further ST depression

with exercise has minimal diagnostic significance. A stable abnormality with exercise is reassuring.

Evidence supporting this recommendation is of classes: C, R

# 110. Do Exercise Imaging Study

When the resting ECG is markedly abnormal, use an exercise imaging test (stress echo, stress radionuclear perfusion, stress radionuclear ventriculogram).

# 111. Do Regular Treadmill Stress Test

Use the Bruce protocol, modified if need be for debilitated patients. Adequacy of exercise and myocardial challenge is generally accepted as achieving greater than or equal to 85% of age-predicted maximum heart rate. The Bruce protocol, because of extensive use and long-term follow-up, provides the most reliable prognostic information.

# 112. Is Test Strongly Positive?

Stress testing may be strongly positive and suggest a moderate to high risk of cardiovascular events as indicated by the Duke treadmill score, which is based upon the Bruce protocol.

A stress test predicts the patient's prognosis and provides evidence of the presence or absence of CAD. Of these two types of information, the first, establishing the patient's prognosis, is the more reliable.

Treadmill findings which signify a poor prognosis are:

- Poor exercise tolerance
- Hypotension
- Marked ST abnormality at a low work load

Conversely, good exercise tolerance to a high heart rate and blood pressure signifies a good prognosis, even if the exercise ECG is somewhat abnormal. (For example, a patient who walks 9 minutes and has 1 mm of asymptomatic ST depression.)

Mark et al (Duke treadmill score) validated an easy-to-use treadmill score which stratifies high-, intermediate-, and low-risk patients. Refer to the NGC summary of the ICSI <u>Cardiac Stress Test Supplement</u> for scoring methods and application.

A Duke score of greater than or equal to five is generally accepted as a passing score, and such patients may be discharged to home with follow-up within 72 hours.

Refer to Appendix E, "Nomogram of the Prognostic Relations Embodied in the Treadmill Score" in the original guideline document.

The Duke treadmill score was developed from a retrospective study of 2,842 inpatients. It was prospectively tested on an outpatient population of 613 patients with an endpoint of patient mortality. Consequently it is the best well-validated measurement for the prognostic interpretation of treadmill tests.

Evidence supporting this recommendation is of classes: A, B, C, R

#### 113. Is Patient a Candidate for Revascularization?

Unless advanced age, comorbidity, or patient preference suggests medical treatment, high-risk patients should be considered for revascularization. Patients identified as high risk by treadmill testing often have left ventricular dysfunction, left main coronary stenosis, or other serious coronary disease. Revascularization may offer a better prognosis.

Evidence supporting this recommendation is of classes: A, C

#### 116. Is Test Positive but Low Risk?

A stress cardiogram may be positive but without features which signify a poor prognosis as noted above. For example, a 65-year-old man with atypical angina and 1.0 mm ST depression at 10 minutes has a good prognosis even though he has coronary disease.

# 117. Is Diagnostic Certainty Adequate?

A positive test may confirm the clinical diagnosis of coronary disease and allow treatment as outlined under the NGC summary of the ICSI guideline Stable Coronary Artery Disease.

Refer to cardiology if diagnostic certainty is critical.

Evidence supporting this recommendation is of classes: C, M

# 120. Is Test Equivocal?

Because of resting abnormality, limited exercise performance, limited heart rate, or minor exercise abnormalities, the test may not be clearly normal or abnormal, yet high-risk treadmill findings are absent.

Evidence supporting this recommendation is of classes: C, M

# 121. Is Diagnostic Certainty Adequate?

Knowing that the patient is not at high risk may suggest empiric treatment or non-cardiac evaluation. Refer to cardiology if diagnostic certainty is important.

Evidence supporting this recommendation is of classes: C, M

#### 124. Test is Normal

A normal test may confirm the clinical impression of non-cardiac symptoms. Refer to cardiology if symptoms are worrisome despite a normal stress test.

Compared with the prognostic information contained in a stress test, the diagnostic information is more variable. The physician must consider:

- 1. How to estimate the pre-test likelihood of coronary disease based upon the patient's age, sex, and description of chest pain. If pretest likelihood is very high or very low, a test of intermediate predictive value, such as treadmill stress testing, may be misleading.
- 2. How abnormal are the exercise findings?

Greater than 1 mm flat or 1.5 mm upsloping ST depression measured 80 msec. after the J point occurring with a normal resting ECG is considered a positive test. However, "positive" is not all-or-nothing. Downsloping ST depression, greater degrees of ST depression, persistent ST depression, and ST depression at a low work load are "more positive." Conversely, upsloping ST depression, ST depression at a high work load, and rapidly-resolving ST depression are "less positive."

- 3. How good is the test itself? Is exercise challenge adequate, heart rate high enough? Resting abnormality present?
- 4. The natural history of a coronary plaque. A non-obstructive plaque may become active, provoke unstable symptoms by platelet emboli or vasoconstriction, yet not impair exercise coronary flow. A normal test isn't reassuring if the symptoms are worrisome.
- 5. What is the diagnostic goal? Absolute certainty for airline pilots? Reasonable reassurance?

Despite the complexities of interpretation, stress testing is a valuable tool in the evaluation of a patient with chest pain. Clinical judgment is paramount.

#### Definitions:

Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

Randomized, controlled trial

Class B:

Cohort study

Class C:

- Non-randomized trial with concurrent or historical controls
- Case-control study
- Study of sensitivity and specificity of a diagnostic test
- Population-based descriptive study

#### Class D:

- Cross-sectional study
- Case series
- Case report
- B. Reports that Synthesize or Reflect upon Collections of Primary Reports:

### Class M:

- Meta-analysis
- Systematic review
- Decision analysis
- Cost-effectiveness analysis

#### Class R:

- Consensus statement
- Consensus report
- Narrative review

# Class X:

Medical opinion

## CLINICAL ALGORITHM(S)

Detailed and annotated clinical algorithms are provided for:

- Chest Pain Screening
- Emergency Intervention
- ST-Segment Elevation Myocardial Infarction (STEMI)
- Acute Myocardial Infarction (AMI) Complications
- Special Work-Up
- Non-Cardiac Causes
- Clinic Evaluation

# EVIDENCE SUPPORTING THE RECOMMENDATIONS

# TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- Successful emergency interventions for patients with high-risk chest pain
- Improved diagnostic value of stress tests through their appropriate use in patients with chest pain symptoms
- Minimized delay in administering thrombolytics or angioplasty to patients with acute myocardial infarction (AMI)
- Appropriate tobacco use assessment and cessation counseling and treatment for patients with AMI
- Appropriate course of treatment for patients with AMI that follows the recommended critical pathway
- Timely initiation of treatment to reduce postinfarction mortality in patients with AMI
- Increased use of risk stratifying procedures in patients with AMI
- Appropriate use of cardiac rehabilitation post-discharge

#### POTENTIAL HARMS

#### Adverse Effects of Medications and Precautions

- The recently completed SYNERGY study found increased adverse events in patients that were switched from unfractionated heparin to low-molecular weight heparin or vice-versa at the time of referral to tertiary care institutions. Therefore, the suggestion is that the patient be started and maintained on one drug or the other during transfer and treatment at referring and referral institutions.
- Low-molecular weight heparin (LMWH) should be used with caution in patients with renal insufficiency.
- Calcium channel blockers should be avoided in patients with decreased left ventricular (LV) function or heart failure. The short-acting dihydropyridine calcium channel blockers (e.g., nifedipine) may be associated with increased risk and should be avoided in acute ischemic syndromes.
- Low patient weight has been identified as an ongoing risk factor for significant intracranial hemorrhage when thrombolytics are administered.
- Use of non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the cardioprotective benefits of aspirin.

# CONTRAINDICATIONS

## **CONTRAINDICATIONS**

#### Contraindications to IIb-IIIa Inhibitors

- Bleeding less than 6 weeks
- Intracranial hemorrhage (ever)
- Recent stroke less than two years
- Uncontrolled hypertension greater than 200/100 mmHg
- Surgery less than six weeks
- Aortic dissection

- Acute pericarditis
- Platelets less than 100,000 mm<sup>3</sup>
- Dialysis dependent renal failure

# Contraindications to Nitroglycerin

- Hypotension
- Documented severe aortic stenosis
- Hypertrophic cardiomyopathy
- Sildenafil, vardenafil, or ordenafil within the previous 24 hours or tadalafil in the previous 48 hours

#### Contraindications to Beta-blockers

#### **Absolute Contraindication**

- ST-elevation myocardial infarction due to cocaine use
- Cardiogenic shock

#### **Relative Contraindications**

- Asthma
- First degree of atrioventricular block
- Hypotension
- Heart rate less than 60/min
- Decompensated congested heart failure

#### Contraindications to Thrombolytics\*

# **Absolute Contraindications**

- Previous hemorrhagic stroke at any time; other strokes or cerebrovascular events within one year
- Known intracranial neoplasm
- Active internal bleeding (does not include menses)
- Suspected aortic dissection

#### Cautions/Relative Contraindications

- Severe uncontrolled hypertension on presentation (greater than 180/110 mm Hg)\*\*
- History of prior cerebrovascular accident or known intracerebral pathology not covered in above absolute contraindications
- Current use of anticoagulants in therapeutic doses (international normalized ration [INR] greater than or equal to 2.0 to 3.0); known bleeding diathesis
- Recent trauma (including head trauma) within 2 to 4 weeks
- Major surgery in past 3 to 6 months
- Noncompressible vascular punctures
- Recent internal bleeding
- For streptokinase/anistreplase: prior exposure (especially within five days to two years) or prior allergic reaction

- Pregnancy
- Active peptic ulcer
- History of chronic hypertension
- \* Advisory only. May not be all inclusive or definitive. Patients with relative contraindications should be evaluated on a case-by-case basis. Percutaneous coronary intervention (PCI) may provide equal or increased benefit at decreased risk.
- \*\*Severe uncontrolled hypertension on presentation is a relative contraindication. Even if hypertension is brought under control, patients subsequently treated with thrombolytics experience increased rates of ICH compared to patients who are normotensive on presentation. Arrange for primary PCI in high-risk hypertensive patients if feasible.

NOTE: Cardiopulmonary resuscitation performed for less than 10 minutes is NOT a contraindication.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

- These clinical guidelines are designed to assist-clinicians by providing an
  analytical framework for the evaluation and treatment of patients, and are not
  intended either to replace a clinician's judgment or to establish a protocol for
  all patients with a particular condition. A guideline will rarely establish the
  only approach to a problem.
- This medical guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients are urged to consult a health care professional regarding their own situation and any specific medical questions they may have.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Once a guideline is approved for general implementation, a medical group can choose to concentrate on the implementation of that guideline. When four or more groups choose the same guideline to implement and they wish to collaborate with others, they may form an action group.

In the action group, each medical group sets specific goals they plan to achieve in improving patient care based on the particular guideline(s). Each medical group shares its experiences and supporting measurement results within the action group. This sharing facilitates a collaborative learning environment. Action group learnings are also documented and shared with interested medical groups within the collaborative.

Currently, action groups may focus on one guideline or a set of guidelines such as hypertension, lipid treatment, and tobacco cessation.

Detailed measurement strategies are presented in the original guideline document to help close the gap between clinical practice and the guideline recommendations. Summaries of the measures are provided in the National Quality Measures Clearinghouse (NQMC).

## Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

- 1. Clinics should have a process in place for a patient to be referred for emergency intervention via 911, or be seen in the clinic the same day, within 72 hours, or as an elective clinic evaluation based upon the presence of high-risk symptoms and duration.
- 2. Hospitals should develop and implement Emergency Department (ED) critical pathways and consider standard orders to accomplish rapid evaluation and treatment of acute coronary syndrome. Standard discharge orders/instructions should also be considered.
- 3. A process should be in place for the patient and family that will rapidly orient them to the suspected diagnosis, ED and Critical Care Unit (CCU) process and other treatment measures to be considered. This could include both caregiver face-to-face interactions with the patient and family as well as teaching tools in written form.
- 4. Institutions that cannot meet the recommended treatment times for primary percutaneous coronary intervention (PCI) should consider the preferential use of intravenous thrombolytics therapy. These institutions should have a predetermined plan for treating patients who present with contraindications to thrombolytics. Such plans may employ delayed local primary PCI or transfer to another institution.

#### **IMPLEMENTATION TOOLS**

Clinical Algorithm
Pocket Guide/Reference Cards
Quality Measures
Resources

For information about <u>availability</u>, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## RELATED NOMC MEASURES

- <u>Diagnosis</u> and treatment of chest pain and acute coronary syndrome (ACS): percentage of patients with chest pain symptoms in emergency department (ED) receiving early therapy including intravenous (IV) access, oxygen, nitroglycerin, morphine and a chewable aspirin on arrival.
- Diagnosis and treatment of chest pain and acute coronary syndrome (ACS): percentage of patients with acute myocardial infarction (AMI) receiving thrombolytics with a "door-to-drug time" (time from presentation to administration of drug) of less than 30 minutes.
- <u>Diagnosis and treatment of chest pain and acute coronary syndrome (ACS):</u> percentage of patients with acute myocardial infarction (AMI) receiving beta-blockers within 24 hours of arrival and on discharge.
- <u>Diagnosis</u> and treatment of chest pain and acute coronary syndrome (ACS): percentage of patients with chest pain symptoms who have had treadmill tests with the Duke score present and aren't high risk.

• <u>Diagnosis and treatment of chest pain and acute coronary syndrome (ACS):</u> <u>percentage of patients with acute myocardial infarction (AMI) receiving or scheduled for a risk stratifying procedure prior to discharge.</u>

# INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

**IOM CARE NEED** 

Getting Better

IOM DOMAIN

Effectiveness Timeliness

## IDENTIFYING INFORMATION AND AVAILABILITY

## BIBLIOGRAPHIC SOURCE(S)

Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of chest pain and acute coronary syndrome (ACS). Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Oct. 76 p. [121 references]

#### **ADAPTATION**

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Nov (revised 2006 Oct)

GUI DELI NE DEVELOPER(S)

Institute for Clinical Systems Improvement - Private Nonprofit Organization

#### GUI DELI NE DEVELOPER COMMENT

Organizations participating in the Institute for Clinical Systems Improvement (ICSI): Affiliated Community Medical Centers, Allina Medical Clinic, Altru Health System, Aspen Medical Group, Avera Health, CentraCare, Columbia Park Medical Group, Community-University Health Care Center, Dakota Clinic, ENT Specialty Care, Fairview Health Services, Family HealthServices Minnesota, Family Practice Medical Center, Gateway Family Health Clinic, Gillette Children's Specialty Healthcare, Grand Itasca Clinic and Hospital, HealthEast Care System, HealthPartners Central Minnesota Clinics, HealthPartners Medical Group and Clinics, Hutchinson Area Health Care, Hutchinson Medical Center, Lakeview Clinic, Mayo Clinic, Mercy Hospital and Health Care Center, MeritCare, Mille Lacs Health System, Minnesota Gastroenterology, Montevideo Clinic, North Clinic, North Memorial Care System, North Suburban Family Physicians, Northwest Family

Physicians, Olmsted Medical Center, Park Nicollet Health Services, Pilot City Health Center, Quello Clinic, Ridgeview Medical Center, River Falls Medical Clinic, Saint Mary's/Duluth Clinic Health System, St. Paul Heart Clinic, Sioux Valley Hospitals and Health System, Southside Community Health Services, Stillwater Medical Group, SuperiorHealth Medical Group, University of Minnesota Physicians, Winona Clinic, Ltd., Winona Health

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#### GUIDELINE COMMITTEE

Cardiovascular Steering Committee

#### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Work Group Members: Steve Mulder, MD (Work Group Leader) (Hutchinson) (Family Medicine); Paul Spilde, PT (Park Nicollet Health Services) (Cardiac Rehabilitation); James Morrison, MD (HealthPartners Medical Group) (Cardiology); Jackson Thatcher, MD (Park Nicollet Health Services) (Cardiology); R. Scott Wright, MD (Mayo Clinic) (Cardiology); Harry D. Malcolm, MD (St. Mary's/Duluth Clinic Health System) (Family Medicine); Jeffrey Garland, MD (St. Mary's/Duluth Clinic Health System) (Hospitalist); Sai Haranath, MD (MeritCare) (Internal Medicine); Kathy Melsha, PharmD (Park Nicollet Health Services) (Pharmacy); Teresa Hunteman (Institute for Clinical Systems Improvement) (Measurement/Implementation Advisor); Ann-Marie Evenson, BS, RHIT (Institute for Clinical Systems Improvement) (Facilitator)

#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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R. Scott Wright, M.D. is a consultant for Pfizer and Merck-Scherling Plough.

No other work group members have potential conflicts of interest to disclose.

ICSI's conflict of interest policy and procedures are available for review on ICSI's website at www.icsi.org.

#### **GUIDELINE STATUS**

This is the current release of the guideline.

This guideline updates a previous version: Institute for Clinical Systems Improvement (ICSI). Diagnosis and treatment of chest pain and acute coronary syndrome (ACS). Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2005 Oct. 78 p.

## GUIDELINE AVAILABILITY

Electronic copies: Available from the <u>Institute for Clinical Systems Improvement</u> (ICSI) Web site.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: <a href="www.icsi.org">www.icsi.org</a>; e-mail: <a href="icsi.info@icsi.org">icsi.info@icsi.org</a>.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Diagnosis and treatment of chest pain and acute coronary syndrome (ACS).
   Executive summary. Bloomington (MN): Institute for Clinical Systems
   Improvement, 2006 Oct. 1 p. Electronic copies: Available from the <u>Institute for Clinical Systems Improvement (ICSI) Web site</u>.
- Health care order set: admission to CCU for acute coronary sydrome.
   Bloomington (MN): Institute for Clinical Systems Improvement, 2006 Oct. 31
   p. Electronic copies: Available from the <u>Institute for Clinical Systems</u>
   <u>Improvement (ICSI) Web site</u>.
- Nomogram of the prognostic relations embodied in the treadmill score.
   Appendix E in the original guideline document. Electronic copies: Available from the ICSI Web site.
- Appendix E Nomogram of the prognostic relations embodied in the treadmill score.
- ICSI pocket guidelines. April 2006 edition. Bloomington (MN): Institute for Clinical Systems Improvement, 2006. 298 p.

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: <a href="www.icsi.org">www.icsi.org</a>; e-mail: <a href="icsi.info@icsi.org">icsi.info@icsi.org</a>.

## PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on February 16, 2005. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal antiinflammatory drugs (NSAIDs). This NGC summary was updated by ECRI on January 12, 2006 and February 1, 2007. This summary was updated by ECRI on March 6, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin sodium). This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on July 12, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Troponin-1 Immunoassay. This summary was updated by ECRI Institute on September 7, 2007 following the revised U.S. Food and Drug Administration (FDA) advisory on Coumadin (warfarin).

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